

Peripatetic health-care workers as potential superspreaders

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Many nosocomial outbreaks exhibit “superspreading events” in which cross-transmission occurs via a single individual to a large number of patients. We investigated how heterogeneity in Health-Care Worker (HCW) behaviors, especially compliance to hand hygiene, may cause superspreading events. In particular, we compared the superspreading potential of peripatetic (noncohorted) HCWs with that of other HCWs. We developed an agent-based model for hand transmission of a pathogen in a hospital ward. Three HCW profiles were allowed: 2 assigned profiles, one with frequent contacts with a limited number of patients, another with fewer contacts but with more patients; and one peripatetic profile, with a single daily contact with all patients. We used data from the literature on common nosocomial pathogens (*Staphylococcus aureus*, *Enterococci*). The average number of patients colonized over 1 month increases with noncompliance to hand hygiene. Importantly, we show that this increase depends on the profile of noncompliant HCWs; for instance, it remains low for a single noncompliant assigned HCW but can be quite large for a single noncompliant peripatetic HCW. Outbreaks with this single fully noncompliant peripatetic HCW (representing only 4.5% of the staff) are similar to those predicted when all HCWs are noncompliant following 23% of patient contacts. Noncompliant peripatetic HCWs may play a disproportionate role in disseminating pathogens in a hospital ward. Their unique profile makes them potential superspreaders. This suggests that average compliance to hygiene may not be a good indicator of nosocomial risk in real life health care settings with several HCW profiles.

hygiene | nosocomial infections | superspreading | agent-based modeling

Over recent years, nosocomial pathogens have become widespread in hospitals worldwide (1, 2), leading to increasingly frequent treatment failures and excess costs (3, 4). Their ability to colonize without causing symptomatic infection amplifies the reservoir of nosocomial pathogens and the risk of patient-patient transmission via transiently colonized health-care workers (HCWs) (5). Control measures such as hand hygiene have proved an effective tool to reduce transmission by HCWs (6). However, individual noncompliant behaviors among HCWs may hamper their efficacy, depending on the frequency and duration of contacts between noncompliant HCWs and patients, as well as on the specific subgroups of patients they visit (6, 7).

On several occasions, nosocomial outbreaks have been traced back to a “peripatetic” HCW, i.e., an HCW having contacts with many patients. For example, an erythromycin-resistant *Staphylococcus aureus* (ERSA) epidemic occurred in a nursery when a single nursing assistant (out of a staff of 45 HCWs) who cared for most of the infants was a carrier of the pathogen (8); a hospital-wide methicillin-resistant *S. aureus* (MRSA) epidemic involving 32 cases was associated with a single respiratory therapist who had chronic sinusitis due to the epidemic strain (9); and several ERSA outbreaks occurring in 2 different hospitals were associated with a single nurse who worked at both hospitals

on alternate weeks (10). Epidemiological data show that many nosocomial outbreaks seem to exhibit such “superspreading events,” where relatively few individuals are responsible for a large part of epidemic transmissions (11–17). The underlying mechanisms of superspreading remain unclear and may involve a combination of host, pathogen, and environmental effects (18). However, increased transmission is bound to be correlated with host activities and behavior, such as hygiene practices, frequency of bodily contacts, tendency to seek treatment, and compliance with control measures (18).

Here, we examine the conditions under which individual noncompliance to hygiene measures among HCWs may lead to superspreading of nosocomial pathogens in a hospital ward. Using an agent-based mathematical model of pathogen transmission, we investigate the impact of HCW profile (daily allocation and schedule and nature of patient contacts) on their superspreading capacity. In particular, we evaluate the superspreading potential of peripatetic HCWs, who are in contact—albeit briefly—with all patients, as opposed to that of other HCWs, who are assigned to a limited number of patients.

Results

We simulated the introduction of a single colonized patient in an 18-bed ward, using an agent-based spatially explicit model of a hypothetical intensive-care unit (ICU) (see *Materials and Methods* and Fig. 1). The ward was supposed previously free from the studied pathogens, for which we investigated a range of transmissibilities, based on data on MRSA and vancomycin-resistant *Enterococci* (VRE).

Three HCW profiles were included in the ward:

(i) Two assigned HCW profiles (AP), the assigned HCW profile 1 (AP1) involving frequent contacts with a limited number of patients—typically a nurse—and the assigned HCW profile 2 (AP2) involving fewer contacts but with more patients—typically a physician.

(ii) One “peripatetic HCW” profile, involving a single daily contact with all patients—for instance a therapist or a radiologist.

From 0 to 5 of all HCWs were supposed noncompliant with hand hygiene recommendations. All possible scenarios were investigated regarding the profile of the noncompliant HCWs among the staff.

Impact of Noncompliance on Pathogen Transmission. Fig. 2 provides the predicted total number of colonized patients (outbreak size) over 1 month according to the number of noncompliant HCWs.

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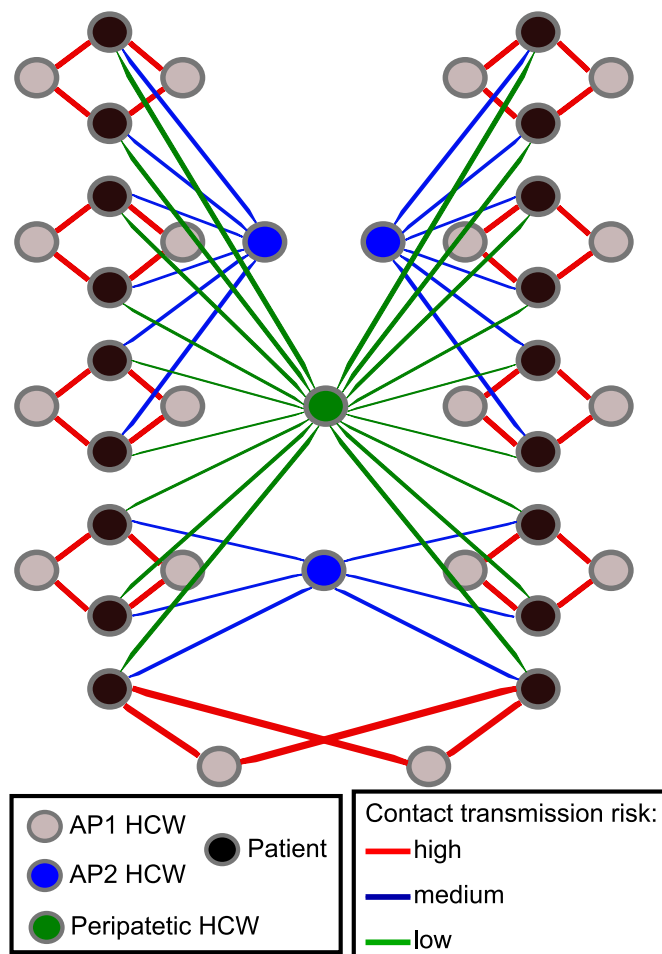


Fig. 1. Network of contacts in the modeled ICU. There are 18 patients (black circles) and 3 types of HCWs: 2 profiles of HCWs assigned to subgroups of patients (assigned profiles 1 and 2, beige and blue circles) and peripatetic-type HCWs (green circles). Per contact transmission risks may be high (investigated range: from 8.5% to 25%, red edges), medium (investigated range: from 5.5% to 17%, blue edges) or low (investigated range: from 3% to 10%, green edges). All contacts are undirected, meaning that transmission may occur in both directions. Patient-AP1 HCWs contacts occur 3 times a day, while other contacts occur once a day.

When all HCWs were compliant, from 1.5 to 5.8 patient cases were predicted over 1 month, depending on pathogen transmissibility. As expected, outbreak size increased with noncompliance; for a single noncompliant HCW, it reached 1.7 to 6.8 patient cases on average over 1 month (a 13 to 17% increase). These results were highly dependent on the profile of the noncompliant HCW, as the increase ranged from 2 to 7% for a noncompliant AP2 HCW and from 73 to 238% for a noncompliant peripatetic HCW.

Importance of the HCW Profile. Fig. 3 depicts the predicted outbreak size over 1 month with the hypothesis of a single noncompliant HCW (assigned profile 1, assigned profile 2, or peripatetic HCW).

The impact of noncompliance was strongest when the peripatetic HCW was noncompliant; the HCW profile was most important for a highly transmissible pathogen. Indeed, the predicted total number of patients colonized over 1 month with the highest investigated transmissibility was approximately 3 times greater with 1 noncompliant peripatetic HCW than with 1 noncompliant assigned HCW (Fig. 3B).

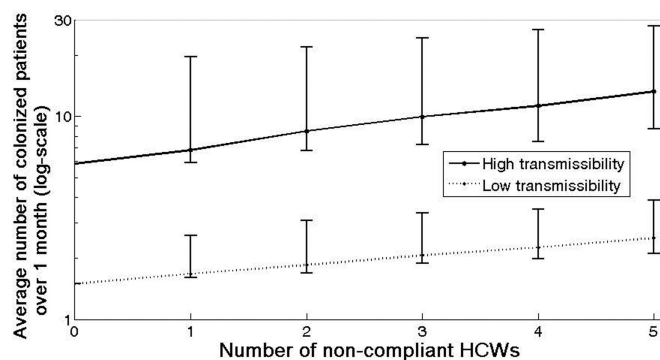


Fig. 2. Total number of patients colonized over 1 month following a single index case (on a log-scale), as a function of the number of noncompliant HCWs. A range of transmissibilities are investigated for the pathogen, from low (dotted line) to high (full line). Lines provide the mean of outbreak sizes computed for all possible scenarios regarding the identity of noncompliant HCWs among the staff. Error bars provide the minimum and maximum among these outbreak sizes.

Comparison with the homogeneous model in which all HCWs had the same equivalent reduced compliance to hand-hygiene (that is, a 4.5% overall reduction in compliance) showed that simulating a single noncompliant assigned HCW led to similar predictions (Figs. 3A and B, left hatched bar). However, a global

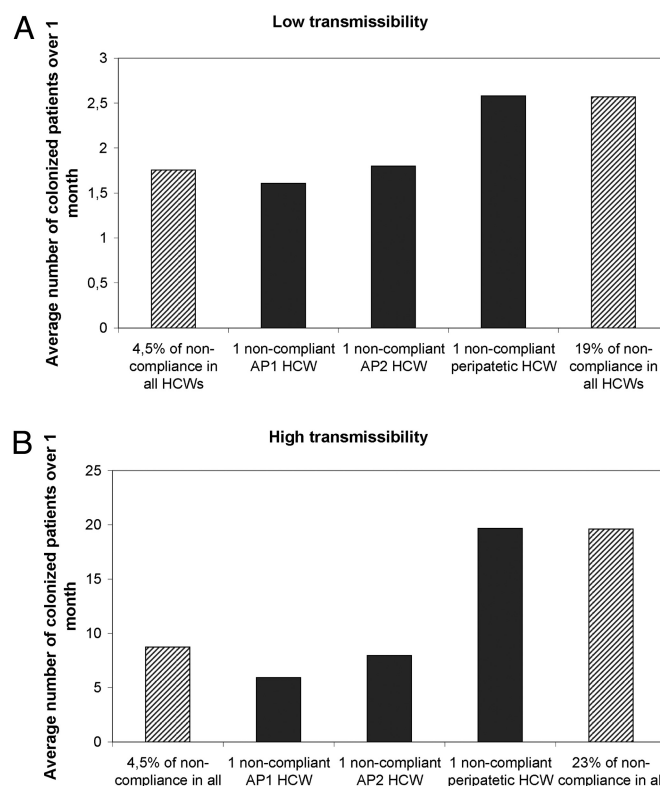


Fig. 3. Total number of patients colonized over 1 month following a single index case, (A) for a low-transmissibility pathogen and (B) for a high-transmissibility pathogen, in the hypothesis of a single noncompliant HCW: assigned HCW (profile 1 or 2) or peripatetic HCW. The total number of patient cases computed in the hypothesis of a homogeneous reduction in compliance among all HCWs is also provided as a reference (left and right hatched bars); the left-hand bar depicts predictions for a 4.5% (= 1/22) homogeneous reduction while the right-hand bar depicts predictions with the homogeneous model that are similar to those obtained with a single peripatetic HCW.

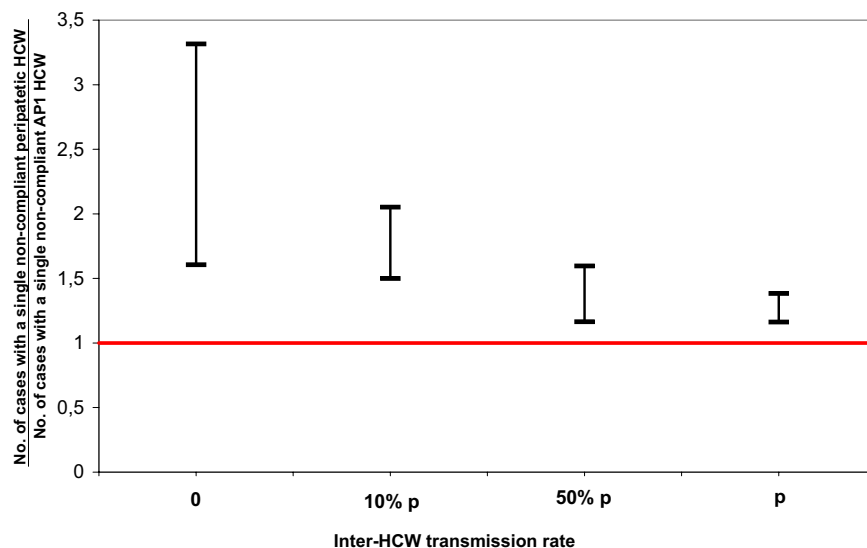


Fig. 4. Impact of HCW-HCW transmissions: results of the sensitivity analysis. The ratio of the total number of patients colonized over 1 month following a single index case predicted in the hypothesis of a single noncompliant peripatetic HCW to the same number predicted in the hypothesis of a single noncompliant assigned HCW (profile 1) is depicted as a function of the per minute rate of transmission between HCWs. This per minute rate of inter-HCW transmission is varied between 0 (no HCW-HCW transmissions) and p (HCW-HCW transmissions as probable as patient-HCW transmissions). For each value of the per-minute rate of inter-HCW transmission, the range of predicted ratios obtained depending on pathogen transmissibility (low to high) is provided.

homogeneous reduction in compliance of up to 23% was needed to reproduce predictions obtained when noncompliant behavior was concentrated in a single peripatetic HCW (Figs. 3 *A* and *B*, right hatched bar).

Similar results were obtained using the probability of transmission of colonization from the index patient to at least one other patient as the outcome (see Figs. S1 and S2).

Analytic Calculations. We performed analytic calculations (*SI Appendix*), which allowed us to compute the expected number of secondary patient colonizations following the introduction of a single index patient in the ward. These calculations confirmed that a noncompliant peripatetic HCW had more impact on the nosocomial risk than a noncompliant assigned HCW and that this difference increased with pathogen transmissibility (Fig. S3). They also allowed the computation of a general criterion on model parameters under which these results held; this criterion could be interpreted as comparing the products of cumulated times at-risk for patient-to-HCW and HCW-to-patient transmissions associated with assigned vs. peripatetic HCW profiles.

Impact of HCW-HCW Transmissions. The results of a sensitivity analysis are depicted in Fig. 4 for transmission rates during HCW-HCW contacts ranging from 0 to p , where p was the per-minute transmission rate during HCW-patient contacts. The predicted total number of cases over 1 month was 1.2 to 3.3 times larger with a noncompliant peripatetic HCW than with a noncompliant assigned HCW, depending on HCW-HCW transmission rates and on pathogen epidemicity (low or high).

Discussion

In this article, we show that systematic noncompliant behavior in a few HCWs may have more impact than a global reduction in compliance in all HCWs. This predicted individual impact should be strongest when the noncompliant individuals are peripatetic HCWs. Peripatetic HCWs appear to have major superspreading potential, especially when the transmitted pathogen is highly epidemic. Our findings may explain several reports of outbreaks that were traced back to peripatetic HCWs (8–10).

Peripatetic HCWs, which we defined as HCWs who pay a single (possibly short) visit to all patients in the ICU daily, can be found among many professions represented in ICUs. Some examples are radiologists and physical therapists or other therapists but also physicians on night duty, staff heads, and so on.

By contrast, the majority of the staff in an average ICU (day and night nurses, interns, or residents, etc.) belongs in the assigned HCW category. However, it should be noted that in conditions of understaffing or overcrowding of the ward, HCWs who usually belong in the assigned HCW category may become peripatetic (noncohorted) HCWs. The influence of HCW cohorting on hand hygiene effectiveness and the consequences of understaffing have been documented in both modeling and observation studies (7, 19, 20). Theoretical modeling work on epidemic diffusion in networks has also shown that the epidemic threshold of infectious diseases is directly related to contact patterns in the community, with diseases spreading more easily among highly connected individuals (21).

An analysis of our model using analytic calculations confirmed our main results (*SI Appendix* and Fig. S3). It further showed that the behavior of our transmission model could be linked to that of host-vectors model (22) with 3 vector types (corresponding to the 3 HCW profiles), and 1 host type (the patients).

HCW Schedule and Allocation. Shadowing studies in American hospitals show that, on average, HCWs spend from 20 to 30% of their working shifts in direct contact with patients, this portion decreasing as the patient-HCW ratio increases (23, 24). Although this varies from one hospital to another, nurses may work 12-h shifts while physicians work shorter shifts (8–9 h) (24); in ICUs, the nurse to patient ratio is often 1:1 to 1:3, while the physician-patient ratio is noticeably lower (25). Furthermore, a detailed analysis of the time spent in direct patient contact suggests that, during these contacts, nurses perform approximately 1.5 more acts that are “at-risk” for pathogen transmission than physicians (24).

Basing our AP1 on nurses and our AP2 on MDs led us to suppose that there were 9 AP1 HCWs for 18 patients during days and 9 others during nights, with each of these AP1 HCWs visiting 2 patients for 25 min 3 times during a 12-h shift, meaning that they spend $2 \times 3 \times 25 / (12 \times 60) = 21\%$ in direct patient contact. Similarly, the 3 AP2 HCWs spend $6 \times 1 \times 25 / (9 \times 60) = 28\%$ of their 9-hour shift in direct patient contact. We also hypothesized that the risk of pathogen transmission was 1.5 times higher during patient contacts with AP1 HCWs.

Alternate schedules and allocations would certainly impact our predictions, as the importance for pathogen transmission of a given HCW increases with the total time he/she spends in patient contact, as well as with the number of patients he/she visits. In particular, the similarity of predictions obtained with a

single noncompliant assigned HCW with profiles 1 and 2 is due to our hypotheses regarding these 2 profiles, which lead to similar daily transmission risks.

Pathogen Colonization and Transmission. Model predictions on pathogen colonization and transmission in the ICU are highly sensitive to variations of 2 parameters: the duration of patient colonization and the transmissibility of the pathogen. Available data allowing the computation of reliable estimates of these parameters are scarce, although a few recent studies have addressed this issue for MRSA (26) or VRE (27).

Regarding colonization duration, the available data suggests carriage may be sustained for very long time periods in the absence of intervention (28), with observed carriage periods of up to 30 months for MRSA for instance. However, in this study, the “colonization duration” parameter is a mean value that incorporates the possibility of carriage detection and subsequent isolation and/or antibiotic treatment of the colonized individual, as well as the effects of constant antibiotic exposure in the ICU. Hence, we fixed this parameter at the arbitrary and much lower value of 10 days. This might, for instance, reflect the impact of weekly systematic bacterial screenings in ICUs, considering that tests for bacterial colonization may take up to 3 days.

To assess model sensitivity to assumed colonization duration, we performed simulations using a 100-day colonization duration, which is closer to reported data for MRSA. Our main results held in these simulations as noncompliance of peripatetic HCWs had more impact than noncompliance of assigned HCWs. What's more, predicted epidemic size over 1 month did not differ significantly from that predicted with a 10 days colonization duration, irrespective of pathogen epidemicity.

Data regarding the existence and duration of acquired immunity due to MRSA colonization is also scarce. Here, we simply assumed that periods of colonization were followed by 3 days during which acquisition of carriage was impossible. This may reflect continuing antibiotic exposure or isolation.

Regarding transmissibility, we used published data on the risk of transmission associated with MRSA or VRE to model 2 pathogens, one with a “low” reference risk of transmission during a standard procedure at around 6% and one with a “high” reference risk of 18% (29–32).

However, the lack of detailed information on pathogen transmission in the ICU has led to several assumptions that may not be realistic. In particular, we chose to consider only patient-HCW transmission in the baseline analysis, thereby neglecting both patient-patient and HCW-HCW transmission, as well as environmental contamination (30). Moreover, we assumed that the risk of transmission was the same from HCW to patient than from patient to HCW, which seems to be contradicted by some studies (29).

Investigation of the Impact of HCW-HCW Transmissions. We assessed the potential impact of HCW-HCW transmissions on our predictions by performing a sensitivity analysis. The results of this analysis showed that our main predictions held even when HCW-HCW transmission was as probable as HCW-patient transmission (Fig. 4) and despite worst-case assumptions on the frequency of HCW-HCW contacts—as we used data from emergency departments rather than from ICUs (23, 24).

Hand Hygiene Efficacy and Compliance. We supposed that hand hygiene was 90% efficient at removing hand carriage in HCWs after contact with a colonized patient. Experimental studies suggest that this efficacy is consistent with the observed reduction following hand hygiene in the hand flora of volunteers, although it may be higher or lower according to the washing or rubbing solution that is used and to the duration and thoroughness of hand hygiene (33, 34).

Regarding compliance of HCWs, we used a highly simplified model of individual behaviors, according to which HCWs were either fully compliant (meaning that they performed systematic hand-hygiene after all patient visits) or not compliant at all. Although this obviously does not reflect reality, we felt it was pertinent as a case-study. Moreover, the 90% efficacy of hand-hygiene can also be seen as reflecting in part a non perfect compliance.

In observance studies of hand hygiene, the reported rate of compliance is about 50% (35), although compliance appears to be significantly higher after patient contacts than before these contacts (36, 37). In our model, a fully compliant HCW is assumed to perform hand hygiene after all patient visits, but never before those visits. Therefore, our baseline scenario of 100% compliance actually reproduces this 50% observed compliance on average, although it constitutes a rather extreme assumption on the distribution of this compliance.

We investigated the effect of this extreme assumption on compliance on our predictions using analytic calculations (*SI Appendix*). This analysis showed that it was actually the most conservative assumption in terms of nosocomial risk, as it led to the smallest predicted number of secondary patient cases among all scenarios with 50% compliance (although this meant that it was also the assumption associated with the greatest absolute effect of noncompliance). It also showed that the criterion on model parameters under which the impact of noncompliance was stronger in peripatetic HCWs than in assigned HCWs remained the same, irrespective of the assumed distribution of the 50% compliance.

Modeling Approach. Mathematical models have long been used to analyze pathogen dissemination in hospital settings, as well as to evaluate various control strategies such as hygiene measures (38, 39). However, most of these models were compartmental models, which best predict disease transmission under conditions of homogeneous mixing and cannot reproduce the spatial intricacies of a hospital ward. Here, we chose to develop an agent-based, spatially explicit model of pathogen transmission in a hypothetical ICU. Agent-based simulation approaches have proven useful in recent years for investigating epidemiological issues such as pandemic influenza or bioterrorism (40, 41). They are well suited for modeling complex phenomena, including the spread of infectious agents, because they account for the stochasticity of biological phenomena and for individual variations, as well as allow for easily integrated time and space heterogeneity (42–44).

What's more, although pathogen dissemination in hospitals has already been described in previous models as a vector-borne infectious process, with HCWs as vectors (38), this work is an attempt to differentiate between different HCW profiles. Again, this was made easier by the agent-based framework.

Conclusions

According to our study, peripatetic HCWs may have major superspreading potential. In particular, this points out that the evaluation of compliance to hygiene measures in hospitals should be done individually rather than globally. For instance, evaluating hand-hygiene compliance through a global indicator such as overall hand rub consumption may not prove sufficient to assess the nosocomial risk (45).

Performing individual surveillance of hand-hygiene compliance should be particularly important when the involved nosocomial pathogen has high epidemicity. This stresses the benefits of investigating the epidemic potential of emerging nosocomial strains as early as possible.

Table 1. Main model parameters

| Model parameter | Assumed value | Reference |
|---|-------------------------------------|---------------------|
| Length of patient stay in the ICU | Gamma distributed with mean 10 days | (43, 44) |
| Patient-to-assigned HCW ratio: | | |
| AP1 HCWs | 2:1 | (24) |
| AP2 HCWs | 6:1 | (24) |
| Peripatetic HCWs | 18:1 | assumed |
| Fraction of time spent in direct patient contact: | | |
| AP1 HCWs | 21% | (22, 23) |
| AP2 HCWs | 28% | (22, 23) |
| Peripatetic HCWs | 50% | assumed |
| Probability of pathogen transmission during a 20 min patient-AP2 HCW or patient-peripatetic HCW contact | 4–14% | (25, 26, 28–31) |
| Probability of pathogen transmission during a 20 min patient-AP1 HCW contact | 7–20% | (23, 25, 26, 28–31) |
| Duration of pathogen colonization in patients before detection and isolation and/or treatment | Gamma distributed with mean 10 days | (27) |
| Hand hygiene efficacy | 90% | (33) |
| Hand hygiene baseline compliance | 50% | (34) |
| Number of noncompliant HCWs (added to baseline) | 0–5 | |

Materials and Methods

An Agent-Based Model of the ICU. We developed and used an agent-based, stochastic, discrete-time, spatially explicit model of a hypothetical ICU. Each patient and HCW was represented as an “agent” with a specific internal state (colonized, temporarily immunized against colonization, etc.) and a geographical situation (room). Every day, the model simulated the actions of each agent, such as patient visits by HCWs. A detailed technical description of the model is available from the authors on request. Here, only details relevant for the investigation of the non compliance issue are provided.

The main model parameters are listed in Table 1.

Organization of the ICU. The hypothetical ICU included 18 single-bed rooms distributed along a single corridor, with a 90% bed occupancy rate. The length of stay in the ICU was set at 10 days (\pm 4 days) (46, 47). Only patient-HCW interactions were modeled in the baseline analysis.

As mentioned earlier, 3 HCW profiles were included:

(i) Two AP, the first one (AP1) involving frequent contacts with a limited number of patients—typically a nurse—and the second one (AP2) involving fewer contacts but with more patients—typically a physician.

(ii) One peripatetic HCW profile, involving a single daily contact with all patients—for instance a therapist or a radiologist.

The model was based on the explicit assignment of each assigned HCW to a specific subpopulation of patients, while peripatetic HCWs were in contact with all patients. During his or her shift, each HCW made a fixed number of visits to each patient in his or her specified population. For example, an AP1 HCW had 3 daily contacts with 2 different patients. Fig. 1 depicts the network of contacts in the simulated ICU.

Characteristics of HCW profiles and their daily schedule and allocation are reported in Table 2.

Pathogen Colonization and Transmission. We simulated the circulation in the ICU of hand-transmitted pathogens such as MRSA and VRE. We chose to investigate a range of transmissibilities for these pathogens, from low to high, as described below.

All between-patients transmissions occurred via HCWs. Following a patient contact, HCWs who did not comply with hygiene measures could be transiently colonized for a few days. We supposed that during a patient-HCW contact, the probability of patient-to-HCW transmission was the same as the probability of HCW-to-patient transmission.

We assumed that the transmission probability scaled with the duration of patient-HCW interactions. Therefore, the probability of transmission during a contact was the product of the per-minute transmission rate multiplied by the duration of the contact. A risk multiplier depending on the nature of the contact and the HCW profile was further applied.

This led us to investigate values ranging from 4 to 12% for a short procedure such as blood collection (12 min; ref. 48), and from 8 to 25% for the insertion of an IV line (25 min; ref. 48), for contacts involving an AP1 HCW. For contacts involving AP2 or peripatetic HCWs, these values ranged from 2.5 to 4% and 5 to 17% for the same procedures.

The duration of patient colonization before decontamination and/or isolation was supposed to follow a Gamma distribution with a 10 days average. These 10 days were followed by 3 days during which acquisition of carriage was impossible (49).

Hygiene Measures: Efficacy and Compliance. Following patient contacts, HCWs could apply standard hygiene procedures. We assumed that these procedures (referred to in the rest of the article as “hand hygiene”) were 90% efficient at removing transient colonization (34). Each HCW could comply with hand hygiene or not. Those who were fully compliant washed their hands following every patient contact. Those who were not compliant never washed their hands.

Table 2. Daily schedule and allocation of the 3 types of health-care workers (HCWs) in the modeled 18-bed ICU: “assigned profile 1” (AP1) HCWs, “assigned profile 2” (AP2) HCWs and “peripatetic profile” HCWs. In all, there are 18 AP1 HCWs (9 during days and 9 during nights), 3 AP2 HCWs and 1 peripatetic HCW

| HCW profile | | Presence in the ICU | Number of patient visits | Duration of patient visits | Risk level of contacts | Number of patients assigned | Contact-at-risk minutes per day ^b |
|-------------|-----------|---------------------|--------------------------|----------------------------|------------------------|-----------------------------|--|
| AP1 | Day AP1 | 7 AM–7 PM | 3 visits/day | 25 min | 1.5 | 2 patients | 225 min |
| | Night AP1 | 7 PM–7 AM | 3 visits/night | 25 min | 1.5 | 2 patients | 225 min |
| AP2 | | 9 AM–6 PM | 1 visit/day | 25 min | 1 ^a | 6 patients | 150 min |
| Peripatetic | | 9 AM–6 PM | 1 visit/day | 15 min | 1 | 18 (all) patients | 270 min |

^aValue taken as reference.

^bCalculated as: number of assigned patients \times duration of patient visits \times daily number of visits per patient \times risk level of contacts.

